Complete Summary

GUIDELINE TITLE

Accelerated radiotherapy for locally advanced squamous cell carcinoma of the head and neck.

BIBLIOGRAPHIC SOURCE(S)

Head and Neck Cancer Disease Site Group. Accelerated radiotherapy for locally advanced squamous cell carcinoma of the head and neck [full report]. Toronto (ON): Cancer Care Ontario (CCO); 2002 Oct [online update]. 19 p. (Practice guideline; no. 5-6c). [26 references]

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SCOPE

DISEASE/CONDITION(S)

Locally advanced (stage III and IV) squamous cell carcinoma of the head and neck (SCCHN)

GUIDELINE CATEGORY

Assessment of Therapeutic Effectiveness
Treatment

CLINICAL SPECIALTY

Oncology
Radiation Oncology

INTENDED USERS

Physicians

GUIDELINE OBJECTIVE(S)

- To determine if accelerated radiotherapy improves loco-regional control or survival compared with conventionally fractionated radiotherapy in patients with newly diagnosed, locally advanced (stage III-IV) squamous cell carcinoma of the head and neck who are deemed suitable for radiotherapy with curative intent
- To evaluate the toxicity associated with accelerated fractionation
- To address whether these regimens enhance the therapeutic ratio comparing benefits to toxicity

TARGET POPULATION

Adult patients with newly diagnosed, locally advanced (stage III-IV) squamous cell carcinoma of the head and neck (SCCHN) who are deemed suitable for radical radiotherapy with curative intent

INTERVENTIONS AND PRACTICES CONSIDERED

Rapid Acceleration of Radiotherapy (delivered in four weeks or less) or Modest Acceleration of Radiotherapy (delivered in six weeks)

1. Accelerated fractionation
2. Accelerated fractionation using a concomitant boost
3. Accelerated fractionation with split course
4. Hyperfractionation

Conventional Radiotherapy Regimens

MAJOR OUTCOMES CONSIDERED

- Survival (overall and disease-free)
- Loco-regional control
- Toxicity
- Change in therapeutic ratio comparing benefits to toxicity

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Hand-searches of Published Literature (Secondary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

November 2000 Guideline

MEDLINE (1966 to November 2000), CANCERLIT (1983 to September 2000) and the Cochrane Library (Issue 3, 2000) were searched with no language restrictions.

"Head and neck neoplasms" (Medical Subject Heading [MeSH]) and "carcinoma, squamous cell" (MeSH) were combined with "fractionation" (MeSH), "dose fractionation" (MeSH), "radiotherapy dosage" (MeSH) and "accelerated" used as a text word. These terms were then combined with the search terms for the following study designs or publication types: practice guidelines, meta-analyses, randomized controlled trials. The citation lists of all retrieved articles were reviewed to identify additional trials. The proceedings of the 1999 and 2000 annual meetings of the American Society of Clinical Oncology (ASCO) and the 1999 annual meeting of the American Society for Therapeutic Radiology and Oncology (ASTRO) were searched for reports of new trials. On-going clinical trials were identified through the Physician Data Query (PDQ) clinical trials database (U.S. National Cancer Institute).

October 2002 Update

MEDLINE (December 2000 to October 2002), the Cochrane Library (Issue 3, 2002), The Physician Data Query (PDQ) clinical trials database, and conference proceedings from 2001 and 2002 were searched for eligible papers and abstracts that have been published since completion of the original guideline report.

Inclusion Criteria

The systematic review was limited to randomized trials and meta-analyses of randomized trials comparing accelerated radiotherapy with a control arm using conventional radiotherapy (daily Monday to Friday). Three-arm trials investigating the addition of chemotherapy or radiosensitizers were included if there was a comparison of accelerated versus conventional treatment and relevant and complete information could be extracted. Overall survival and loco-regional control were the primary outcomes of interest. Change in the therapeutic ratio comparing benefits to toxicity was also considered.

NUMBER OF SOURCE DOCUMENTS

November 2000 Guideline

Eleven randomized trials (12 comparisons) met the inclusion criteria.

October 2002 Update

Four published reports and three meeting abstracts have become available since the original guideline was completed.

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Expert Consensus (Committee)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Not applicable

METHODS USED TO ANALYZE THE EVIDENCE

Meta-Analysis of Randomized Controlled Trials
Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

The results for survival and loco-regional control were pooled in separate analyses using the Metaanalyst[0.998] software provided by Dr. Joseph Lau (Boston, MA). The Head and Neck Cancer Disease Site Group decided that it would be appropriate to conduct a pooled analysis because the patient populations were similar and the treatment groups were comparable. Data from the total randomized population were pooled if available. Otherwise, data from the evaluable patients were used. Data were abstracted from published reports. The random effects model was used as the more conservative estimate of effect. Results were expressed as risk ratios (RR) with 95% confidence intervals (CI). A risk ratio less than 1.0 favours the experimental treatment (accelerated radiotherapy) and a risk ratio greater than 1.0 favours the control (conventional radiotherapy).

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

A draft report on altered fractionation in locally advanced squamous cell carcinoma of the head and neck (SCCHN) was submitted to the Head and Neck Cancer Disease Site Group (DSG). Subsequent feedback from DSG members suggested that there was too much information to be considered in a single guideline. Therefore, two guidelines were developed, one addressing hyperfractionated radiotherapy and the second addressing accelerated radiotherapy. It was suggested that both guidelines include a reference to the recently completed guideline on concomitant chemotherapy and radiation in the same group of patients.

The DSG members expressed regret that the trial of modest acceleration reported by Overgaard et al could not be included in the pooled analysis because of incomplete information. The author has been contacted to obtain data on the number of patients and rate of loco-regional failure in each arm, but there has been no response to date. The pooled analysis, as presented in the guideline, probably underestimates the potential for improved loco-regional control with accelerated radiotherapy.

The DSG members agreed that rapid acceleration of radical radiotherapy produced unacceptable normal tissue toxicity and could not be recommended as standard therapy.

In comparing the relative merits of hyperfractionation and accelerated fractionation in patients with locally advanced disease, the DSG members noted that there was evidence for improved loco-regional control for both strategies.

However, the group rated modestly accelerated regimens somewhat higher because they could improve the therapeutic index without undue pressure on departmental resources. It was acknowledged that the delivery of daily radiation six or seven times per week could pose logistical difficulties in some Canadian centres.

Given the strength of the data supporting concomitant chemoradiation as summarized in the Care Care Ontario Practice Guideline Initiative (CCOPGI) practice guideline on concomitant chemotherapy and radiotherapy in SCCHN, the DSG members concluded that concomitant chemoradiation should be regarded as the treatment of first choice in patients with locally advanced SCCHN. It would be reasonable to offer modestly accelerated radiotherapy to patients with locally advanced disease who were not judged to be candidates for concomitant chemoradiation. For most centres, this goal could be most reliably achieved with the concomitant boost protocol of the Radiotherapy Oncology Group (RTOG).

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

External Peer Review
Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Practitioner feedback was obtained through a mailed survey of 112 practitioners in Ontario (15 medical oncologists, 25 radiation oncologists and 72 surgeons). The survey consisted of 21 items evaluating the methods, results, and interpretive summary used to inform the draft recommendations and whether the draft recommendations should be approved as a practice guideline. Written comments were invited. Follow-up reminders were sent at two weeks (post card) and four weeks (complete package mailed again). The results of the survey have been reviewed by the Head and Neck Cancer Disease Site Group.

The approved practice guideline recommendations reflect the integration of the draft recommendations with feedback obtained from the external review process.

Final approval of the original guideline report was obtained from the Practice Guidelines Coordinating Committee.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

- This group of patients should be considered for concomitant chemotherapy and conventional radiation as recommended in Cancer Care Ontario Practice Guideline Initiative Guideline No. 5-6a titled "Concomitant Chemotherapy and Radiotherapy in Squamous Cell Head and Neck Cancer (Excluding Nasopharynx)" (See the National Guideline Clearinghouse [NGC] summary).
- It would be reasonable to offer modestly accelerated radiotherapy to patients with locally advanced (stage III and IV) disease who are not candidates for concomitant chemotherapy and conventional radiation.
- Rapid acceleration of radical radiotherapy cannot be recommended as standard therapy.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

November 2000 Guideline

Eleven randomized trials (12 comparisons) of accelerated radiotherapy compared with conventional radiotherapy met the inclusion criteria. Five of these trials have been published only in abstract form. Data on loco-regional response, loco-regional control and survival are summarized in Table 2 (see the original guideline document). The four-arm Radiation Therapy Oncology Group trial 9003 deserves special consideration because of the simultaneous comparison of accelerated, hyperfractionated and conventionally fractionated regimens (see Table 3 in the original guideline document).

October 2002 Update

Since the original guideline was completed in November 2000, new evidence has become available from four published reports and three meeting abstracts. None of these describe new randomized trials.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Modest acceleration of radical radiotherapy without an accompanying reduction in total dose may be superior to conventional fractionation. A reduction in overall treatment time from seven weeks to six weeks achieved by delivering six fractions per week instead of five fractions per week, or by treating patients seven days a week instead of five days per week, or using a concomitant boost over the last 12 treatment days, yielded improved loco-regional control with increased but manageable acute toxicity. Full data on long-term effects are not yet available, but based on the limited evidence that is available from randomized trials the effects appear to be clinically acceptable.

POTENTIAL HARMS

Rapid acceleration of radical radiotherapy results in excessive normal tissue toxicity. This can be minimized by reducing the total dose (as in the continuous hyperfractionated accelerated radiotherapy [CHART] regimen) or introducing a treatment interruption (as in the split-course protocols of the European Organization for Research and Treatment of Cancer trial 22811 and the Radiation Therapy Oncology Group trial 9003) but at the expense of tumour control. These regimens have not proven superior to conventional fractionation in terms of survival and loco-regional control.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

- The emerging evidence suggests that modestly accelerated radiotherapy can improve loco-regional control compared with conventional radiotherapy. Overall survival may be enhanced. Although the improvements in loco-regional control and survival are promising, longer follow-up and more complete information on late complications will be needed to meaningfully compare these results to those achieved with concomitant chemoradiation in locally advanced squamous cell carcinoma of the head and neck.
- Care has been taken in the preparation of the information contained in this document. Nonetheless, any person seeking to apply or consult these guidelines is expected to use independent medical judgment in the context of individual clinical circumstances or seek out the supervision of a qualified clinician. Cancer Care Ontario makes no representation or warranties of any kind whatsoever regarding their content or use or application and disclaims any responsibility for their application or use in any way.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Living with Illness

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

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ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2000 Nov 27 (updated online 2002 Oct)

GUIDELINE DEVELOPER(S)

Practice Guidelines Initiative - State/Local Government Agency [Non-U.S.]

GUIDELINE DEVELOPER COMMENT

The Practice Guidelines Initiative (PGI) is the main project of the Program in Evidence-based Care (PEBC), a Province of Ontario initiative sponsored by Cancer Care Ontario and the Ontario Ministry of Health and Long-Term Care.

SOURCE(S) OF FUNDING

Cancer Care Ontario, Ontario Ministry of Health and Long-Term Care

GUIDELINE COMMITTEE

Head and Neck Cancer Disease Site Group

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

For a current list of members, please see the Cancer Care Ontario Web site.

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Members of the Head and Neck Cancer Disease Site Group disclosed potential conflict of interest information.

GUIDELINE STATUS

This is the current release of the guideline.

The FULL REPORT, initially the full original Guideline or Evidence Summary, over time will expand to contain new information emerging from their reviewing and updating activities.

Please visit the Cancer Care Ontario Web site for details on any new evidence that has emerged and implications to the guidelines.

GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) from the Cancer Care Ontario Web site.

AVAILABILITY OF COMPANION DOCUMENTS

The following is available:

- Accelerated radiotherapy for locally advanced squamous cell carcinoma of the head and neck. Summary. Toronto (ON): Cancer Care Ontario (CCO), 2000 Nov 27 (revised 2002 Oct). Electronic copies: Available in Portable Document Format (PDF) from the Cancer Care Ontario Web site.

The following companion guidelines are also available:

- Concomitant chemotherapy and radiotherapy in squamous cell head and neck cancer (excluding nasopharynx). Toronto (ON): Cancer Care Ontario (CCO), 2000 Mar. Various p. (Practice guideline; no. 5-6a). See the National Guideline Clearinghouse (NGC) summary.
- Hyperfractionated radiotherapy for locally advanced squamous cell carcinoma of the head and neck. Toronto (ON): Cancer Care Ontario (CCO), 2000 Nov. Various p. (Practice guideline; no. 5-6b). See the National Guideline Clearinghouse (NGC) summary.

PATIENT RESOURCES

None available

NGC STATUS

This summary was completed by ECRI on June 5, 2002. The information was verified by the guideline developer as of July 8, 2002. This summary was updated on August 6, 2003. The updated information was verified by the guideline developer on September 2, 2003.

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